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90% identity with the sequence of a leptin and has the ability to block cell proliferation.--

## REMARKS

Claims 2-9 and 28-39 presently appear in this case. No claims have been allowed. The official action of June 21, 2000, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method for treating tumors in mammals or for inhibiting tumor cell proliferation in mammals by administering to a mammal in need thereof an effective amount of leptin or a mutein, fragment, or fusion protein thereof, or a leptin receptor agonist which has the ability to block cell proliferation.

Claims 1-9 have been rejected under 35 U.S.C. §101 because the claimed recitation of a use without setting forth any steps results in an improper definition of process.

Claim 1 has now been deleted in favor of new claim 28 which is written in method claim form. Claims 2-9 have been amended to appear in method claim form and to depend from claim 28. Accordingly, this rejection has now been obviated.

Claims 19-27 have been objected to because they are dependent on process claims in an improper format. Claims 19-27 have now been deleted, thus obviating this objection. All of the present claims are in a proper format.

Claims 1-27 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The examiner states that claims 1-9 are vague and indefinite in the term "use of an inactive agent".

Claim 1 has now been deleted and claims 2-9 have been amended to be method claims, rather than use claims. Thus, this part of the rejection has now been obviated.

The examiner states that claims 1 and 10 recite "active fragments or fractions of any one thereof, active analogs or derivatives of any one thereof ... and mixtures of any therefore". The examiner states that the defining activity of the claimed active agent is unclear and, therefore, the nature of the claimed analogs and derivatives is unclear.

Claims 1 and 10 have now been deleted. New claim 28 now recites the active fragments, analogs, etc., specifying that the defining activity is the ability to block cell proliferation. Accordingly, it is submitted that this ground of rejection no longer applies to new claim 28.

The examiner states that claims 11-17 recite an intended use, but it is unclear how the intended use modifies the claimed active agent.

Claims 11-17 have now been deleted, thus obviating this part of the rejection.

The examiner states claims 20-25 recite an intended use, but it is unclear how the intended use modifies the claimed pharmaceutical composition.

Claims 20-25 have now been deleted, thus obviating this part of the rejection.

The examiner states that in claim 19 the language "an active agent according to claim 1" lacks proper antecedent basis.

Claim 19 has now been deleted, thus obviating this part of the rejection.

It is submitted that all of the claims now present in the case now fully comply with 35 U.S.C. §112, second paragraph. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 1-27 have been rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for leptin and leptin fusion proteins, does not reasonably provide enablement for leptin muteins, leptin receptor agonists, active fragments or fractions, active analogs or derivatives and mixtures. The examiner states that the specification provides only examples and guidance for the use of leptin as an inhibitor of the phosphorylation of insulin receptor substrate-1, and one of ordinary skill in the art would not know what changes in the leptin sequence could

be tolerated by the leptin receptor with respect to JAK-2 activation. Therefore, the examiner concludes that practice of the invention to the full scope of the claims would require undue experimentation to make and use substances other than leptin or leptin fusion proteins. This rejection is respectfully traversed.

New claim 28 specifies the use of leptin in paragraph (a) and leptin fusion proteins in paragraph (d). However, it is submitted that the muteins of paragraph (b), fragments of paragraph (c) and agonists of paragraph (e) are also fully supported by the present specification, and those of ordinary skill in the art could practice the present invention without undue experimentation. The muteins have been defined at page 8, line 19, to page 9, line 3, as well as page 13, first full paragraph. The active fragments are defined at page 14, lines 21-25; and the agonists are described in the paragraph bridging pages 14 and 15. Salts and functional derivatives are described in the paragraph bridging pages 13 and 14 and in the following paragraph. Thus, those of ordinary skill in the art reading the present specification would know how to make each of these proteins or fragments or agonists and test them for cell proliferation blocking activity by means of the assay described in the specification. While some experimentation would be necessary,

this would not be undue experimentation. In this regard, reference is made to the Revised Interim Written Description Guidelines Training Materials, Example 9, with respect to hybridization, and Example 14, with respect to percent identity. It can be seen that present PTO practice is to accept a certain degree of breadth with respect to muteins despite lack of specific examples. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 1-6, 8-15, 17 and 18 have been rejected under 35 U.S.C. §102(a) as being anticipated by Rubinstein (Cytokine, 1997). This rejection is respectfully traversed.

The form PTO-892, which the examiner uses to cite this reference, indicates that the date of the abstract is November 1997. All of the present claims are entitled to the effective filing date of applicants' Israeli priority application 120733, filed April 29, 1997. The priority application is in the English language and is of record in the case in view of the fact that it was filed in the course of the PCT proceeding of which the present application is a national phase. It is requested that the examiner review this priority document in order to confirm that applicants are entitled to the effective filing date of this application for all of the present claims, thus obviating this rejection. In

any event, Rubinstein is a publication of the present inventors and, if necessary, a declaration can be prepared by Rubinstein, Barkan and Cohen confirming that Novick, while a co-author of the abstract, is not an inventor of the present application. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 1, 2, 7 and 16 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Rubinstein in view of Jackson (1998). This rejection is also respectfully traversed.

Rubinstein is not available as a reference for the reasons discussed above. Jackson is not available as a reference for the same reason. It is dated April 1998, and the present application was filed in April 1998, and it is entitled to an effective filing date of its Israeli priority application filed in April 1997. Reconsideration and withdrawal of this rejection are, therefore, also respectfully urged.

Claim 24 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Rubinstein and Jackson and further in view of Stephens. This rejection is respectfully traversed.

As Rubinstein and Jackson are not available as references, this rejection must fall for the same reasons as

the previous rejection discussed above. Reconsideration and withdrawal of this rejection are, therefore, also respectfully urged.

Claims 19-23 and 25-27 have been rejected under 35 U.S.C. §103(a) as unpatentable over Rubinstein in view of Stephens. This rejection is respectfully traversed.

Rubinstein is not available as reference. Therefore, this rejection must fall for the same reasons as discussed above with respect to the other rejections.

It is submitted that all the claims now present in the case fully comply with 35 U.S.C. §112 and clearly define over the references of record. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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